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Early systemic inflammatory response after ultrasound-guided percutaneous liver mass biopsy: Role of hematologic parameters

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Abstract

The acute inflammatory response to tissue damage from percutaneous liver biopsy has not been systematically characterized in the immediate post-procedural period. This study investigated changes in hematologic parameters during the early period following ultrasound-guided liver mass biopsies, focusing on the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) as inflammatory markers. A total of 127 patients who underwent ultrasound-guided liver mass biopsy between January 2015 and March 2018 were retrospectively reviewed. Complete blood counts were obtained from blood samples taken before and 4 hours after the procedure. NLR was calculated by dividing the neutrophil count by the lymphocyte count, and PLR by dividing the platelet count by the lymphocyte count. Based on pathology results, patients were categorized as having malignant (n=117) or benign (n=10) liver lesions. Pre- and post-procedure values were compared. The mean age of the patients was 66.9 ± 13.3 years. Post-procedurally, the median NLR increased from 2.68 to 3.19 ($p<0.001$), and median PLR increased from 137 to 152 ($p=0.008$). NLR increased in 64.6% of patients, and PLR increased in 57.5%. An increase of more than 30% from baseline was observed in 40.9% of patients for NLR and in 35.4% for PLR. Additionally, a significant decrease in hemoglobin levels (mean decrease of 0.6 g/dL) was observed ($p<0.001$). The research results maintained their statistical power after the Bonferroni correction was applied to account for multiple comparisons. A significant early systemic inflammatory response occurs following percutaneous liver biopsy. Increases in NLR and PLR values support this observation. We conducted the first investigation which measured NLR and PLR values during the first four hours after patients underwent percutaneous liver biopsy. The clinical value of these changes requires future studies to validate their effects on patient outcomes because a clear association with improved patient outcomes has not been established.

Keywords: Biopsy, needle, hematologic tests, inflammation, liver neoplasms

Introduction

Liver diseases stand as major contributors to death rates and illness statistics throughout the world. Primary liver cancer is the fifth most common cancer globally and the third leading cause of cancer-related deaths [1]. The medical community considers liver biopsy as the definitive method for diagnosing and monitoring chronic liver diseases. The most commonly used method for the histopathological evaluation of focal liver lesions is percutaneous liver biopsy [2]. The prognostic value of inflammatory markers derived from blood tests has become more significant for diagnosing liver diseases during recent years. Two such markers, the neutrophil-to-lymphocyte ratio (NLR) and the platelet-to-lymphocyte ratio (PLR), have been shown to assist in predicting clinical outcomes in conditions such as hepatocellular carcinoma, liver cirrhosis, and non-alcoholic fatty liver disease [3,4]. These markers have become essential in clinical practice, as they show body-wide inflammation and are easily obtainable through standard blood tests [5].

Current data on the complication rates and safety profile of liver biopsy are limited and somewhat inconsistent [6]. Most existing studies focus on the prognostic value of long-term inflammatory markers in chronic liver diseases, and there is limited information in the literature on the role of these markers in the acute phase following invasive procedures [7,8]. The research community has studied NLR and PLR as predictive indicators for liver diseases and cancers but their behavior following liver biopsy

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procedures has not been systematically investigated. The tissue damage caused by biopsy may trigger systemic inflammatory responses, which could be reflected in hematologic parameters. Monitoring these changes may help clinicians anticipate early complications and better understand the body's immediate reaction to the procedure.

This study was based on the hypothesis that tissue injury caused by percutaneous liver mass biopsy induces a measurable systemic inflammatory response, detectable through routine blood tests. Specifically, it aimed to evaluate early variations in the NLR and PLR following ultrasound-guided liver biopsy, and to assess their potential clinical significance in the immediate post-procedural period. The research presents original findings about how NLR and PLR values change during the initial four hours after patients undergo percutaneous liver biopsy. This study examines the immediate post-procedure inflammatory response associated with this commonly performed medical procedure through its first four hours of observation.

Material and Methods

Study Population and Sample

We conducted this retrospective observational study, which included consecutive patients who underwent ultrasound-guided percutaneous liver mass biopsy at our hospital between January 2015 and March 2018. The research followed STROBE guidelines for observational studies to conduct and present its findings. The researchers used G*Power 3.1 software (Heinrich Heine University, Düsseldorf, Germany) to determine the required number of participants. Based on the neutrophil-lymphocyte ratio (NLR) changes and standard deviations reported in the literature after similar invasive procedures [9,10], it was determined that a minimum of 120 patients should be included to obtain 80% power at a 5% significance level using a paired-tailed t-test with an expected effect size of d=0.52.

The inclusion criteria for the study were as follows: having undergone a liver mass biopsy, having complete blood count data available before the procedure and at the 4th hour after the procedure, and having a confirmed histopathological diagnosis. Patients with missing hemogram data, signs of concurrent systemic infection, those who had received granulocyte colony-stimulating factor or high-dose corticosteroid therapy within the last four weeks, those who underwent another invasive procedure on the same day, and patients with known hematological malignancy were excluded from the study. Of the 165 patients initially evaluated, 127 who met these criteria were included in the study (Figure 1). The NLR was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count, and the PLR was calculated by dividing the platelet count by the absolute lymphocyte count. Delta values were obtained by subtracting the pre-procedure value from the post-procedure value. The researchers established a 30% increase above baseline values as their definition for significant change because this threshold is commonly used for studying short-term inflammatory reactions in medical research [11,12].

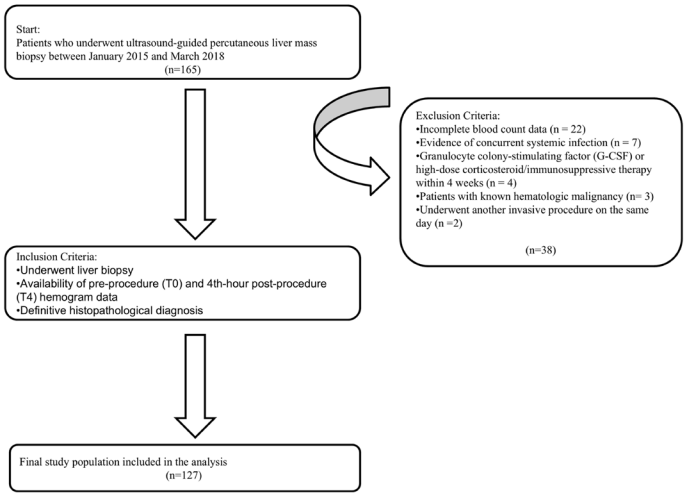

Figure 1. Flow chart of patient selection and exclusion process

Study Procedures

Data were collected retrospectively from the hospital electronic medical record system. Demographic information, clinical characteristics, and laboratory results were recorded on standardized data forms. Complete blood count measurements were performed on venous blood samples taken no later than 24 hours before the procedure and at 4 hours (±30 minutes) after the procedure. The researchers selected this 4-hour observation period because it matches the typical post-procedural monitoring duration used at our institution for patient observation before releasing them from the hospital. The present research period allows detection of the beginning of acute inflammation which emerges after the first few hours following tissue damage [12,13].

All hematological analyses were performed on the same device throughout the study period: Sysmex XN-1000 hematology analyzer (Sysmex Corporation, Kobe, Japan). Histopathological diagnoses were made by experienced pathologists and classified as malignant or benign. Malignant cases were grouped according to subtypes: metastatic disease, hepatocellular carcinoma, cholangiocarcinoma, and other malignancies. Metastatic disease was detected in 74%, hepatocellular carcinoma in 11%, cholangiocarcinoma in 6%, and other malignancies in 9% of the primary diagnosis distribution.

Interventional Protocol

All biopsy procedures were performed in the interventional radiology unit by interventional radiologists with at least 5 years of experience using the coaxial technique under ultrasound guidance (Figure 2). Patients were placed in the supine position, the biopsy site was covered with sterile drapes, and local anesthesia with lidocaine was administered to the skin and subcutaneous tissue.

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The liver capsule was penetrated with a 17-gauge coaxial biopsy needle, and tissue specimens were obtained using an 18-gauge Bard® Magnum™ fully automatic tru-cut biopsy needle (Bard Biopsy Systems, Tempe, AZ, USA). With the coaxial system, a single skin entry was made, and the coaxial needle was advanced and fixed approximately 1 cm short of the target lesion. Through the stabilized coaxial sheath, the tru-cut biopsy gun was fired three times to obtain samples from both the peripheral and more central regions of the lesion, yielding three tissue specimens per patient. After the procedure, all patients were observed for 4 hours. As per institutional protocol, patients were kept nil per os for 4 hours before the procedure. The medical team provided intravenous hydration through 0.9% saline solution (which totaled about 500 mL) to all patients throughout the observation time. The patient received oral paracetamol (500-1000 mg) for post-procedural pain relief but healthcare providers skipped non-steroidal anti-inflammatory drugs because they could interfere with platelet function.

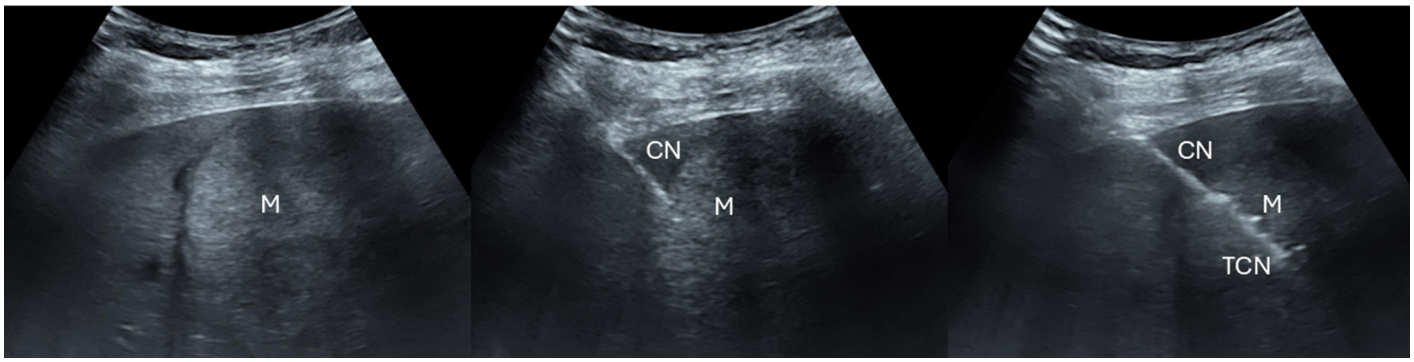

Figure 2. Ultrasound-guided percutaneous liver mass biopsy (M: liver mass; CN: coaxial needle; TCN: tru-cut biopsy needle)

Statistical Analysis

Data analysis was performed using SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Normally distributed data were presented as mean (SD), and non-normally distributed data were presented as median [first-third quartiles]. Categorical variables were expressed as counts and percentages. The paired t-test was used for normally distributed data, and the Wilcoxon signed-rank test was used for non-normally distributed data to compare pre- and post-procedure values. The Mann-Whitney U test and Fisher's exact test were applied to compare malignant and benign groups. Spearman correlation analysis was used to examine relationships between variables. Values of 3 for NLR and 150 for PLR were determined as clinically significant threshold values based on the literature [14].

The current cut-off values were developed from research which predicted hepatocellular carcinoma and chronic liver disease development but their effectiveness for acute post-biopsy periods has not been evaluated. An increase of 30% or more from baseline was used as the criterion for clinical significance of the inflammatory response. Missing data were excluded from the analysis, and the evaluation was performed on the complete data set. P values were calculated bilaterally, and $p<0.05$ was considered statistically significant. Given the multiple comparisons performed, Bonferroni correction was applied for the six primary hematological comparisons (adjusted $\alpha=0.0083$). The research included a sensitivity analysis which removed data points that exceeded three standard deviations from the mean to verify the stability of the results. The G*Power 3.1 software performed post-hoc power analysis to evaluate the malignant versus benign subgroup differences because the two groups contained different numbers of participants (117 vs 10). Due to the small sample size in the benign group, these subgroup analyses were considered exploratory.

Ethical Considerations

This study was approved by the Corporate Ethics Committee of Medline Hospitals (Approval No: 07, Date: June 11, 2025). Owing to the retrospective design, the requirement for informed consent was waived by the committee. Patient privacy was safeguarded through anonymization and coding of data. Data were stored on encrypted, password-protected computers and in databases accessible only to the study team. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

The mean age of the 127 patients included in the study was 67 years. The distribution of female and male patients was similar, with women showing a slight predominance. Malignant lesions were detected in the majority of patients, while benign pathologies were quite rare. Metastatic liver disease was the most common malignant diagnosis, followed by hepatocellular carcinoma and cholangiocarcinoma. Changes in hematological parameters were observed in blood samples taken before the biopsy procedure and at 4 hours. The neutrophil numbers rose after the procedure but lymphocyte numbers dropped. The procedure resulted in a major decrease of hemoglobin values but platelet counts remained unchanged. The NLR was around 3 before the procedure and approached 4 after the procedure. There was a similar increase in the PLR (Table 1, Figure 3).

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Table 1. Patient characteristics and hematological parameters

Parameter	Value/T0 (Before)	T4 (Post)	p value
Demographic characteristics			
Age, years (mean ± SD)	66.9 ± 13.3	-	-
Age, years (median [IQR])	69.0 [60.0-75.0]	-	-
Gender - Female, n (%)	65 (51.2%)	-	-
Gender - Male, n (%)	62 (48.8%)	-	-
Pathology - Malignant, n (%)	117 (92.1%)	-	-
Pathology - Benign, n (%)	10 (7.9%)	-	-
Hematological parameters			
Neutrophils, $\times 10^9$/L (median [IQR])	5.54 [4.07-7.56]	5.88 [4.35-8.43]	<0.001*
Lymphocytes, $\times 10^9$/L (median [IQR])	1.66 [1.23-2.33]	1.48 [1.04-2.00]	0.002*
Hemoglobin, g/dL (mean ± SD)	12.20 ± 2.15	11.60 ± 2.09	<0.001†
Platelets, $\times 10^9$/L (median [IQR])	227 [176-321]	224 [159-313]	0.087*
NLR (median [IQR])	3.13 [2.11-4.76]	3.82 [2.57-6.34]	<0.001*
PLR (median [IQR])	137 [97-195]	152 [109-232]	0.008*

*Wilcoxon signed-rank test, †Paired t-test, NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio; IQR: interquartile range; T0: baseline (before procedure); T4: 4 hours after procedure; SD: standard deviation

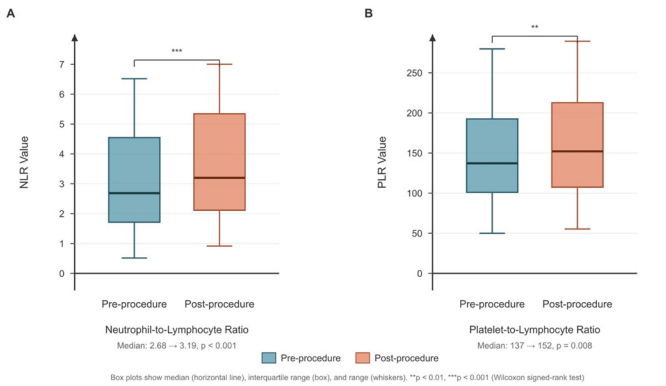

Figure 3. Pre- and Post-Procedure NLR and PLR Values. (A) NLR, (B) PLR. Box plots show median, interquartile range, and range. NLR: neutrophil-to-lymphocyte ratio; PLR: platelet-to-lymphocyte ratio. **p<0.01, ***p<0.001

When evaluating the inflammatory response after the procedure, an increase in the NLR was observed in two-thirds of the patients. An increase in the PLR occurred in slightly more than half of the patients. When increases above 30%, which is considered clinically significant, were examined, this level of increase in the NLR was detected in two-fifths of the patients, and in the PLR in more than one-third. While the NLR was above 3 in half of the patients before the procedure, this ratio increased to two-thirds after the procedure. Specifically, 17 patients (13.4%) newly exceeded the NLR greater than 3 threshold after the procedure. The number of patients with a PLR exceeding the threshold value of 150 also increased similarly, with 11 patients (8.7%) newly exceeding this threshold post-procedure. The NLR values showed an 18.2% median change which fell within an IQR range of -8.5 to 52.1. The PLR values experienced a median change of 4.8% which spanned from -14.2 to 31.5.

When comparing malignant and benign groups, the changes were positive in the malignant group [median ΔNLR: 0.58 (IQR: -0.25 to 1.95); median ΔPLR: 8 (IQR: -20 to 49)], whereas there was a negative trend in the benign group [median ΔNLR: -0.07 (IQR: -0.82 to 0.45); median ΔPLR: -3 (IQR: -38 to 22)]. The malignant group included 67.5% of patients who had elevated NLR values, whereas the benign group contained only 30.0% of patients with elevated NLR values (p=0.028). However, due to the small number of benign patients, most of the differences were not statistically significant when comparing malignant and benign lesions in terms of inflammatory response. The post-hoc power analysis showed that the study achieved only low statistical power to detect malignant versus benign group differences, which varied between 18% and 41% for different parameters. The research findings from these comparisons should be considered preliminary results (Table 2).

A weak positive correlation was found between the change in the NLR and the change in the PLR when examining the relationships between the variables (r=0.218, p=0.014). There was a strong negative relationship between the change in the PLR and the change in platelet count (r=-0.674, p less than 0.001), which is expected because mathematically, the ratio increases as the platelet count decreases; this correlation is presented as a consistency check rather than an independent biological finding. When pre- and post-procedure values were evaluated among themselves, a strong positive correlation was found in both the NLR (r=0.698, p less than 0.001) and the PLR (r=0.812, p less than 0.001). This indicates that patients with high values at baseline tended to have high values after the procedure (Table 3).

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Table 2. Inflammatory response and subgroup analysis

Parameter	All patients (n=127)	Malignant (n=117)	Benign (n=10)	p-value‡
Inflammatory changes				
ΔNLR (median [IQR])	0.52 [-0.31 to 1.88]	0.58 [-0.25 to 1.95]	-0.07 [-0.82 to 0.45]	0.412
ΔPLR (median [IQR])	6 [-23 to 47]	8 [-20 to 49]	-3 [-38 to 22]	0.523
% Change in NLR (median [IQR])	18.2% [-8.5 to 52.1]	19.8% [-7.2 to 54.3]	-2.1% [-24.5 to 15.8]	0.385
% Change in PLR (median [IQR])	4.8% [-14.2 to 31.5]	5.6% [-13.1 to 33.2]	-2.4% [-22.8 to 18.6]	0.498
Increase in NLR, n (%)	82 (64.6%)	79 (67.5%)	3 (30.0%)	0.028§
Increase in PLR, n (%)	73 (57.5%)	70 (59.8%)	3 (30.0%)	0.095§
NLR increase >30%, n (%)	52 (40.9%)	50 (42.7%)	2 (20.0%)	0.196§
PLR increase >30%, n (%)	45 (35.4%)	43 (36.8%)	2 (20.0%)	0.497§
Clinical threshold values				
NLR >3 (T0), n (%)	66 (52.0%)	62 (53.0%)	4 (40.0%)	0.517§
NLR >3 (T4), n (%)	83 (65.4%)	79 (67.5%)	4 (40.0%)	0.095§
PLR >150 (T0), n (%)	54 (42.5%)	51 (43.6%)	3 (30.0%)	0.517§
PLR >150 (T4), n (%)	65 (51.2%)	62 (53.0%)	3 (30.0%)	0.196§
New cases exceeding NLR >3, n (%)	17 (13.4%)	17 (14.5%)	0 (0.0%)	0.361§
New cases exceeding PLR >150, n (%)	11 (8.7%)	11 (9.4%)	0 (0.0%)	1.000§

Values are presented as median [IQR] or number (%). Δ: post-procedure minus pre-procedure value; T0: before procedure, T4: 4 hours after procedure. NLR: neutrophil-to-lymphocyte ratio, PLR: platelet-to-lymphocyte ratio, IQR: interquartile range. ‡Mann-Whitney U test for continuous variables; §Fisher's exact test for categorical variables. Due to the small sample size in the benign group (n=10), comparisons between malignant and benign groups are exploratory and should be interpreted with caution. Post-hoc power analysis indicated approximately 22% power to detect a medium effect size (d=0.5) for these comparisons

Table 3. Correlation analysis

Variables	Correlation coefficient (r)*	p value
ΔNLR vs ΔPLR	0.218	0.014
ΔNLR vs age	-0.087	0.331
ΔPLR vs age	-0.134	0.134
ΔNLR vs ΔHemoglobin	-0.102	0.254
ΔPLR vs ΔPlatelet†	-0.674	<0.001
NLR T0 vs NLR T4	0.698	<0.001
PLR T0 vs PLR T4	0.812	<0.001

*Spearman correlation coefficient. †The correlation between ΔPLR and ΔPlatelet is mathematically expected given the definition of PLR (Platelet/Lymphocyte) and is presented as a consistency check rather than an independent biological finding. Δ=post-procedure minus pre-procedure value; T0=before procedure; T4=4 hours after procedure. NLR=neutrophil-to-lymphocyte ratio; PLR=platelet-to-lymphocyte ratio. Primary diagnosis distribution among malignant patients: metastatic disease 73.5%, hepatocellular carcinoma 11.1%, cholangiocarcinoma 6.0%, other 9.4%

The research team conducted supplementary statistical tests to verify the stability of their observed results. The Bonferroni correction for multiple comparisons produced statistically significant results for neutrophils, lymphocytes, hemoglobin, NLR, and PLR, but the platelet count change remained not statistically significant (adjusted α=0.0083). The research included a sensitivity analysis which removed data points that fell outside three standard deviations from the mean. The results showed no change after removing 5 patients who had values that fell outside ±3 standard deviations: the median ΔNLR value stayed at 0.48 while the median ΔPLR value remained at 5 and the NLR increase rate continued at 63.1%. The essential research findings from our study remained valid, as all primary comparisons showed the same statistical significance (Table 4).

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Table 4. Statistical corrections and sensitivity analysis

A. Multiple comparison correction (Bonferroni)			
Comparison	**Original p-value**	**Bonferroni-corrected p-value***	**Significance†**
Neutrophils (T0 vs T4)	<0.001	<0.006	Significant
Lymphocytes (T0 vs T4)	0.002	0.012	Significant
Hemoglobin (T0 vs T4)	<0.001	<0.006	Significant
Platelets (T0 vs T4)	0.087	0.522	Not significant
NLR (T0 vs T4)	<0.001	<0.006	Significant
PLR (T0 vs T4)	0.008	0.048	Significant
B. Post-hoc power analysis for malignant vs benign comparison			
Parameter	**Effect size (Cohen's d)**	**Achieved power‡**	**Required n for 80% power**
ΔNLR	0.38 (Small-Medium)	22%	n=220 (110 per group)
ΔPLR	0.31 (Small)	18%	n=328 (164 per group)
NLR increase rate	0.76 (Medium-Large)	41%	n=56 (28 per group)
PLR increase rate	0.60 (Medium)	32%	n=90 (45 per group)
C. Sensitivity analysis: Excluding extreme values (±3 SD)			
Parameter	**Original result**	**After exclusion (n=122)**	**Conclusion**
ΔNLR (median)	0.52	0.48	Result stable
ΔPLR (median)	6	5	Result stable
NLR T0 vs T4 (p-value)	<0.001	<0.001	Result stable
PLR T0 vs T4 (p-value)	0.008	0.011	Result stable
NLR increase rate (%)	64.6%	63.1%	Result stable
PLR increase rate (%)	57.5%	56.6%	Result stable

*Bonferroni correction applied for 6 primary comparisons (adjusted α=0.05/6=0.0083). †Significance determined at corrected α level of 0.0083. ‡Post-hoc power calculated using G*Power 3.1 with observed effect sizes and actual sample sizes (malignant n=117, benign n=10), α=0.05, two-tailed. Cohen's d effect size interpretation: small (0.2), medium (0.5), large (0.8). The low statistical power for malignant-benign comparisons confirms that these analyses should be considered exploratory. Future studies with larger benign cohorts are warranted

Discussion

In this study, we investigated the systemic inflammatory response associated with percutaneous liver mass biopsies performed under ultrasound guidance in the early period. Both the NLR and PLR demonstrated significant alterations within 4 hours after the procedure. The majority of patients exhibited elevated inflammatory markers, suggesting that percutaneous liver biopsy may trigger a measurable systemic inflammatory response. The body shows typical acute phase response signs through elevated neutrophil numbers and decreased lymphocyte counts following tissue damage. The research presents the first measurements of NLR and PLR changes which occur during the initial hours after percutaneous liver biopsy procedures. This study provides new information about the rapid inflammatory response which occurs during standard medical procedures involving liver biopsies.

The acute changes in NLR and PLR detected in the early period after percutaneous liver biopsy are important indicators of the systemic inflammatory response following invasive procedures. The marked increase in the median NLR value is consistent with similar studies in the literature. The available research about percutaneous liver biopsy does not include direct comparisons but other minimally invasive procedures have been studied for their relevant information. Zhao et al. demonstrated that the increase in NLR after elective percutaneous coronary intervention was associated with periprocedural complications, but they did not report specific median value changes as in our study [10]. Research on kidney biopsy procedures which share similar levels of invasiveness has demonstrated that these procedures produce similar early blood test results. The study by Moledina and colleagues showed that percutaneous renal biopsy resulted in a 0.7 g/dL decrease in hemoglobin, which was comparable to our study results (0.6 g/dL), but they did not measure NLR

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and PLR inflammatory markers [15]. The meta-analysis which combined data from multiple studies about CT-guided lung biopsy procedures found that the overall rate of complications ranged from 24% to 39% based on the biopsy method used, while pneumothorax and hemorrhage occurred as the primary adverse events [16].

The lower increase in NLR in our findings, compared to major surgical procedures, can be explained by the fact that liver biopsy is a less invasive procedure and therefore triggers a lesser systemic inflammatory response. The route of access during transjugular liver biopsy procedures may influence the inflammatory response, but no comparative studies are available that compare this method to percutaneous biopsy procedures [17,18].

Our findings in hematological parameters reflect distinct components of the systemic response following liver biopsy. The increase in neutrophil count is associated with the acute inflammatory response to tissue trauma. Liu and colleagues have noted that neutrophil infiltration plays a critical role in inflammation and tissue damage in liver diseases [19]. The reduction in lymphocytes indicates that the body shifts these cells as part of its stress response which triggers cortisol release. The procedure-induced minimal blood loss together with blood volume expansion explains the decrease in hemoglobin levels. The 0.6 g/dL decrease in hemoglobin levels could have resulted from hemodilution caused by intravenous fluids which patients received during the observation period in addition to blood loss from the procedure. Bissonnette and colleagues conducted a research study to determine the bleeding risks following liver biopsy through both clinical and laboratory tests. The researchers used ultrasonographic findings of liver hematomas and new free fluid or a drop in hemoglobin levels by 2 g/dL or more to diagnose bleeding [20]. The stable platelet numbers confirmed that our patients did not experience major bleeding complications. The guidelines from Neuberger and colleagues indicate that liver disease patients require more than platelet count and prothrombin time measurements to determine their coagulation status. Our findings suggest that platelet stability may be associated with the absence of complications [21].

The increase in the proportion of patients exceeding the NLR >3 and PLR >150 thresholds in our study highlights the clinical significance of the post-biopsy inflammatory response. In advanced hepatocellular carcinoma, Naviwala and colleagues used an NLR threshold value of >2.72. They reported that the median survival time for patients above this value was five months (95% CI: 4-11 months), while it was 13 months (95% CI: 9-32 months) for patients below this value [22]. The threshold values were developed through studies of liver disease and cancer prognosis but their application in post-procedure acute care environments requires further validation. The increase in NLR in 64.6% of our patients supports the idea that biopsy may be an inflammatory trigger. The research results showed statistical significance in NLR and PLR analysis which remained stable after Bonferroni correction for multiple comparisons. An increase in PLR was observed in our findings (median 137 to 152, p=0.008), which can be explained by the acute tissue trauma induced by the biopsy procedure. Niu et al. reported that the combined NLR–PLR score predicted prognosis after liver transplantation, with patients scoring 2 having a median overall survival of 6 months [23]. Our findings demonstrate that inflammatory markers can exceed clinical threshold values even in percutaneous liver biopsy, emphasizing the importance of monitoring this situation.

The analysis requires careful interpretation of the strong negative association which exists between ΔPLR and Δplatelet count ($r=-0.674$, $p<0.001$). The mathematical relationship between PLR and platelet and lymphocyte counts exists because PLR values are derived from dividing platelet numbers by lymphocyte numbers. The PLR value will decrease when platelet numbers decrease because of this calculation method. The researchers present this result as a consistency check rather than evidence of a new biological phenomenon, and it should not be overinterpreted.

The small sample size of the benign group may be related to the lack of statistical significance in inflammatory response differences between malignant and benign groups. Post-hoc power analysis revealed that the achieved statistical power for detecting differences between groups ranged from 18% to 41%, indicating that these comparisons are underpowered and should be considered exploratory. Castiglione and colleagues reported that NLR increased significantly at 72 hours after TAE in HCC patients and returned to baseline levels at 30 days [24]. Our findings revealed that the dynamic changes in NLR and PLR values (ΔNLR and ΔPLR) were positive in the malignant group and negative in the benign group. The NLR values of patients demonstrated a greater increase in the malignant group than in the benign group since 67.5% of malignant patients showed NLR growth but only 30.0% of benign patients did (p=0.028). The extent of inflammatory response seems to depend on the specific medical condition which affects patients. The research needs additional studies with bigger sample sizes because the current study included only ten participants in the benign group. The high correlations between baseline and post-procedure NLR values ($r=0.698$) and PLR values ($r=0.812$) are consistent with the findings of Minici et al., suggesting that the baseline inflammatory status may be important in predicting post-procedural inflammatory burden [19]. It was observed that the inflammatory response was more pronounced in malignant lesions; however, further studies with larger and more balanced cohorts are warranted to validate this observation.

This study has several limitations that should be acknowledged. First and most importantly, the small number of patients in the benign lesion group limited the ability to make valid comparisons with the malignant group. Second, the retrospective design created challenges for data standardization, introduced potential selection bias, and limited our ability to control for confounding factors. The researchers excluded 38 patients

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from the study because their hemogram test results were missing, which may have introduced additional selection bias. The research failed to obtain long-term follow-up data, which prevented the tracking of inflammation patterns through time and identifying when complications could emerge. The study lacks a control group which consists of patients who received no biopsy procedure because this prevents researchers from identifying changes that result from biopsy procedures versus those that stem from fasting duration or hospital stress or normal leukocyte patterns throughout the day. The 4-hour measurement time point shows only the initial stage of the inflammatory response but studies indicate that inflammatory markers reach their highest levels between 12 and 48 hours after tissue damage, so multiple measurements throughout a longer time span would have shown the full inflammatory process. The study failed to obtain systematic data about clinical results which included post-procedural pain measurements and bleeding incidents that needed medical assistance and infection occurrences and patients' length of hospital stay. The clinical relevance of the observed changes therefore remains to be established. The available data on analgesic use did not allow researchers to determine whether pain-related cortisol production led to neutrophilia and lymphopenia independently of the biopsy procedure. The research used threshold values derived from different clinical studies, but these values have not been validated for post-biopsy patients (NLR>3, PLR>150,>30% increase).

Despite these limitations, our study stands out as one of the few investigations that thoroughly evaluates the initial inflammatory responses which occur following biopsy procedures. The strengths of the study include the inclusion of all consecutive patients using a standard technique by experienced specialists at the same center, the use of a coaxial technique ensuring procedural uniformity, and the performance of hematological analyses on the same device throughout the study period, minimizing analytical variability. The application of Bonferroni correction for multiple comparisons and sensitivity analysis excluding outliers helps to confirm the main results of our study.

The results require further validation to establish their medical value, but doctors need to recognize that percutaneous liver biopsy causes an immediate inflammatory response which affects the entire body. The upcoming research needs to concentrate on six main areas which include: (1) Studies which monitor patients over time using multiple measurement points at 4, 12, 24, 48 and 72 hours to study complete inflammatory patterns. (2) The study needs to include a control group to determine how biopsy procedures affect patients. (3) The research needs to establish links between NLR and PLR measurement changes and patient outcomes, including pain symptoms and bleeding incidents and infection rates and hospital stay duration. (4) The research should evaluate how different biopsy methods (percutaneous versus transjugular) affect patient inflammatory responses. (5) The research needs to enroll more participants with benign conditions to achieve sufficient power for studying malignant versus benign disease differences. (6) The research needs to establish procedure-specific thresholds which indicate the occurrence of major procedure-related complications.

Conclusion

Significant changes in inflammatory markers occur during the early period following percutaneous liver mass biopsy. Both the NLR and PLR increase as part of the immediate systemic inflammatory response to the procedure. The clinical significance of these changes together with their relationship to treatment results has not been proven yet. A better understanding of how these changes influence patient outcomes is needed to clarify their clinical value in monitoring.

The research indicates that patients with existing cancer tumors might develop stronger inflammation, but the present study results do not support any particular warning levels for medical practice. The implementation of NLR and PLR monitoring for routine practice requires future research to establish both the specific thresholds which indicate complications and the patient groups who face elevated complication risks and the cost-effectiveness of this monitoring approach. Scientists require detailed research on inflammatory changes because they need to determine if these changes occur as physiological tissue responses to damage or if they indicate prognostic elements. The study shows that percutaneous liver biopsy triggers an immediate body-wide inflammatory reaction, which requires further investigation to establish its value for modifying post-biopsy patient treatment plans.

Ethical Approval
Approved by the Corporate Ethics Committee of Medline Hospitals (No: 07; Date: 11 June 2025).

Patient Consent
Informed consent was waived due to the retrospective design.

Conflict of Interest
The authors declare no conflict of interest.

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